(FILE 'HOME' ENTERED AT 13:50:16 ON 24 SEP 2002)

FILE 'REGISTRY' ENTERED AT 13:50:38 ON 24 SEP 2002

FILE 'CAPLUS' ENTERED AT 13:50:44 ON 24 SEP 2002
S CUCUCGCACCCATCTCTCTCCUUCU/SQSN

FILE 'REGISTRY' ENTERED AT 13:51:49 ON 24 SEP 2002
L1 325 S CUCUCGCACCCATCTCTCTCCUUCU/SQSN

FILE 'CAPLUS' ENTERED AT 13:57:11 ON 24 SEP 2002
L2 118 S L1
L3 70 L2 AND ANTISENSE
L4 5 L3 AND INTERNUCLEOTIDE LINKAGE
L5 5 L3 AND METHYLPHOSPHONATE
L6 2 L3 AND ALKYLPHOSPHONATE

08887687 Serial #

6458940 allowable claims

HPV specific oligonucleotides

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:566652 CAPLUS
DOCUMENT NUMBER: 135:163318
TITLE: Human papillomavirus gene E1 antisense oligonucleotides for HPV inhibition, detection, and therapy
INVENTOR(S): Robert, Peter C.; Frank, Bruce L.; Szymkowski, David E.; Mills, John S.; Goodchild, John; Wolfe, Jia L.; Kilkuskie, Robert E.; Greenfield, Isobel M.; Sullivan, Veronia
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 471,974.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001010899	A1	20010802	US 1997-887497	19970702
US 2002068820	A1	20020606	US 1995-471974	19950606
PRIORITY APPLN. INFO.:			US 1995-471974 A2	19950606
			US 1996-21041P P	19960702

AB The present invention discloses synthetic oligonucleotides complementary to a nucleic acid spanning the translational start site of human papillomavirus gene E1,and including at least 15 nucleotides. Also disclosed are methods and kits for inhibiting the replication of HPV, for inhibiting the expression of HPV nucleic acid and protein, for detection of HPV, and for treating HPV infections. In some embodiments, these oligonucleotides are modified. In one embodiment, the modifications comprise at least one internucleotide linkage selected from the group consisting of **alkylphosphonate**, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester, including combinations of such linkages, as in a chimeric oligonucleotide. In other modifications, the oligonucleotides of the invention may also include at least one deoxyribonucleotide, at least one **ribonucleotide**, or a combination thereof, as in a hybrid oligonucleotide. In a particular embodiment, the oligonucleotide may consist of deoxyribonucleotides only. An oligonucleotide contg. at least one **2'-O-Me ribonucleotide** is one embodiment of the invention. Emphasis is given to oligonucleotides contg. phosphorothioate linkages, RNA-DNA hybrid regions, **2'-O -Me** RNA regions, 5-methyl-cytosine, amino propanol caps, **2'-O-Me** caps, and cholesteryl or polyethylene glycol linkers.

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:374664 CAPLUS
DOCUMENT NUMBER: 122:123152
TITLE: Oligonucleotide analogs containing **ribonucleotide alkylphosphonates** or alkylphosphonothioates and their use as pharmaceuticals
INVENTOR(S): Kandimalla, Ekambar R.; Temsamani, Jamal; Agrawal, Sudhir
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417093	A1	19940804	WO 1994-US902	19940125
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2154578	AA	19940804	CA 1994-2154578	19940125
AU 9461654	A1	19940815	AU 1994-61654	19940125
EP 677056	A1	19951018	EP 1994-908639	19940125
EP 677056	B1	19960522		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1121721	A	19960501	CN 1994-191393	19940125
AT 138384	E	19960615	AT 1994-908639	19940125
ES 2086997	T3	19960701	ES 1994-908639	19940125
JP 08508714	T2	19960917	JP 1994-517287	19940125
FI 9503541	A	19950831	FI 1995-3541	19950724
PRIORITY APPLN. INFO.:			US 1993-9262	19930125
			WO 1994-US902	19940125

AB Disclosed is an oligonucleotide analog comprising at least one **ribonucleotide alkylphosphonate** or alkylphosphonothioate. This analog is preferably from 2 to 60 nucleotides in length and has at least one **ribonucleotide** substituted at the 2' position of its ribose group. Also disclosed are therapeutic formulations comprising this oligonucleotide analog, methods of inhibiting the expression of a gene from a virus, pathogenic organism, or cell, the expression of which is assocd. with a disease state, and methods of treating a mammal infected with a virus or pathogenic organism or afflicted with a disorder resulting from the expression of a cellular gene. Oligonucleotide CTCTCGCACCCATCTCTCTCCUUCT, contg. methylphosphonate linkages between the first 20 nucleotides and phosphodiester linkages between the remaining nucleotides and contg. **2'-O-Me** groups on residues 21-24, was prepd. and characterized. The methylphosphonate modification did not hinder duplex formation with complementary DNA or RNA nor did it significantly destabilize the duplexes formed. The modified oligonucleotide was 8-9-fold more resistant to snake venom phosphodiesterase than was the control oligonucleotide.

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:566652 CAPLUS
DOCUMENT NUMBER: 135:163318
TITLE: Human papillomavirus gene E1 antisense oligonucleotides for HPV inhibition, detection, and therapy
INVENTOR(S): Robert, Peter C.; Frank, Bruce L.; Szymkowski, David E.; Mills, John S.; Goodchild, John; Wolfe, Jia L.; Kilkuskie, Robert E.; Greenfield, Isobel M.; Sullivan, Veronia
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 471,974.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001010899	A1	20010802	US 1997-887497	19970702
US 2002068820	A1	20020606	US 1995-471974	19950606

PRIORITY APPLN. INFO.: US 1995-471974 A2 19950606
US 1996-21041P P 19960702

AB The present invention discloses synthetic oligonucleotides complementary to a nucleic acid spanning the translational start site of human papillomavirus gene E1,and including at least 15 nucleotides. Also disclosed are methods and kits for inhibiting the replication of HPV, for inhibiting the expression of HPV nucleic acid and protein, for detection of HPV, and for treating HPV infections. In some embodiments, these oligonucleotides are modified. In one embodiment, the modifications comprise at least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester, including combinations of such linkages, as in a chimeric oligonucleotide. In other modifications, the oligonucleotides of the invention may also include at least one deoxyribonucleotide, at least one **ribonucleotide**, or a combination thereof, as in a hybrid oligonucleotide. In a particular embodiment, the oligonucleotide may consist of deoxyribonucleotides only. An oligonucleotide contg. at least one **2'-O-Me ribonucleotide** is one embodiment of the invention. Emphasis is given to oligonucleotides contg. phosphorothioate linkages, RNA-DNA hybrid regions, **2'-O-Me** RNA regions, 5-methyl-cytosine, amino propanol caps, **2'-O-Me** caps, and cholesteryl or polyethylene glycol linkers.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:612461 CAPLUS
DOCUMENT NUMBER: 127:304370
TITLE: Interstrand crosslinking reaction in transplatin-modified oligo-**2'-O-methyl ribonucleotide**-RNA hybrids
AUTHOR(S): Colombier, Caroline; Boudvillain, Marc; Leng, Marc
CORPORATE SOURCE: Centre de Biophysique Moleculaire, CNRS, Orleans, 45071, Fr.
SOURCE: Antisense & Nucleic Acid Drug Development (1997), 7(4), 397-402
CODEN: ANADF5; ISSN: 1087-2906
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the context of developing an approach to irreversibly and specifically

link oligonucleotides to RNA, the purpose of this work was to det. the factors interfering with the rate of the rearrangement of the transplatin 1,3-intrastrand crosslinks into interstrand crosslinks, rearrangement triggered by the formation of a double helix between platinated oligo-**2'-O-methyl-ribonucleotides** and their complementary strands. The rate of the rearrangement was studied as a function of the length of the hybrids, the location of the intrastrand crosslinks, the nature of the oligonucleotide backbone, and the nature of the doublet replacing the triplet complementary to the intrastrand crosslinks. The thermal stability of the platinated hybrids was detd. in various salt conditions. The results are discussed in relation to the mechanism of the rearrangement. It is shown that the cellular proteins present weaker nonspecific interactions with single-stranded platinated oligo-**2'-O-methyl**-nucleotides than with the isosequential oligodeoxyribonucleotides.

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:374664 CAPLUS
DOCUMENT NUMBER: 122:123152
TITLE: Oligonucleotide analogs containing **ribonucleotide** alkylphosphonates or alkylphosphonothioates and their use as pharmaceuticals
INVENTOR(S): Kandimalla, Ekambar R.; Temsamani, Jamal; Agrawal, Sudhir
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417093	A1	19940804	WO 1994-US902	19940125
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2154578	AA	19940804	CA 1994-2154578	19940125
AU 9461654	A1	19940815	AU 1994-61654	19940125
EP 677056	A1	19951018	EP 1994-908639	19940125
EP 677056	B1	19960522		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1121721	A	19960501	CN 1994-191393	19940125
AT 138384	E	19960615	AT 1994-908639	19940125
ES 2086997	T3	19960701	ES 1994-908639	19940125
JP 08508714	T2	19960917	JP 1994-517287	19940125
FI 9503541	A	19950831	FI 1995-3541	19950724
PRIORITY APPLN. INFO.:			US 1993-9262	19930125
			WO 1994-US902	19940125

AB Disclosed is an oligonucleotide analog comprising at least one **ribonucleotide** alkylphosphonate or alkylphosphonothioate. This analog is preferably from 2 to 60 nucleotides in length and has at least one **ribonucleotide** substituted at the 2' position of its ribose group. Also disclosed are therapeutic formulations comprising this oligonucleotide analog, methods of inhibiting the expression of a gene from a virus, pathogenic organism, or cell, the expression of which is assocd. with a disease state, and methods of treating a mammal infected with a virus or pathogenic organism or afflicted with a disorder resulting from the expression of a cellular gene. Oligonucleotide CTCTCGCACCCATCTCTCTCCUUCT, contg. **methylphosphonate** linkages

between the first 20 nucleotides and phosphodiester linkages between the remaining nucleotides and contg. **2'-O-Me** groups on residues 21-24, was prepd. and characterized. The **methylphosphonate** modification did not hinder duplex formation with complementary DNA or RNA nor did it significantly destabilize the duplexes formed. The modified oligonucleotide was 8-9-fold more resistant to snake venom phosphodiesterase than was the control oligonucleotide.

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L11 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:772125 CAPLUS
DOCUMENT NUMBER: 135:313608
TITLE: Modified antisense oligonucleotides for inhibition of vascular endothelial growth factor synthesis and treatment of skin disorders
INVENTOR(S): Smyth, Adrienne P.; Robinson, Gregory S.
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 629,730, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6306829	B1	20011023	US 1996-761708	19961206
US 5641756	A	19970624	US 1995-569926	19951208
US 6399586	B1	20020604	US 1999-320911	19990527

PRIORITY APPLN. INFO.:

US 1995-569926	A2	19951208
US 1996-629730	B2	19960409
US 1993-98942	A2	19930727
US 1995-378860	A2	19950126
US 1995-398945	A2	19950302
US 1996-761708	A1	19961206
US 1998-124304	B1	19980729

AB Disclosed are oligonucleotides complementary to VEGF-specific nucleic acid useful in reducing the expression of VEGF. Also disclosed are pharmaceutical formulations contg. such oligonucleotides useful for treating various disorders assocd. with neovascularization and angiogenesis, and methods for treating psoriasis. Modified oligonucleotides complementary to nucleotides in the region 58-90 of vascular endothelial growth factor (VEGF) gene that inhibit hypoxia or transforming growth factor .alpha. induction of VEGF synthesis are described for use in the treatment of proliferative disorders including those assocd. with neovascularization and angiogenesis, and psoriasis. The backbone of the oligonucleotide may include ribose, 2'-deoxyribose, or **2'-O-alkyl** ribose, or modified internucleoside linkages, e.g., phosphorothioate linkages. Antisense oligonucleotides of the invention inhibited VEGF synthesis and lowered levels of VEGF mRNA in cultures of U373 human glioblastoma cells and normal human epidermal keratinocytes. Matrigel.RTM. implants of U373 glioblastoma cells showed lowered levels of vascularization and hemorrhage when anti-VEGF antisense oligonucleotides were incorporated into the matrix.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:401992 CAPLUS
DOCUMENT NUMBER: 133:57578
TITLE: Cancer cell vaccine employing MHC class II Ii protein expression regulators
INVENTOR(S): Xu, Minzhen; Qiu, Gang; Humphreys, Robert
PATENT ASSIGNEE(S): Antigen Express, Inc., USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000034467	A1	20000615	WO 1999-US28096	19991124
W: AU, CA, CN, JP, KR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6368855	B1	20020409	US 1998-205995	19981204
EP 1135482	A1	20010926	EP 1999-961831	19991124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1998-205995	A	19981204
US 1996-661627	A1	19960611
US 1998-36746	B2	19980309
WO 1999-US28096	W	19991124

AB Disclosed is a specific regulator of MHC class II Ii (invariant chain) protein expression or immunoregulatory function. Specifically disclosed are several forms of the specific regulator of Ii, including those which function through the formation of a duplex mol. with an RNA mol. encoding mammalian Ii protein to inhibit Ii protein synthesis at the translation level. This class includes copolymers comprised of nucleotide bases which hybridize specifically to the RNA mol. encoding mammalian Ii protein, and also expressible reverse gene constructs. In other aspects, the disclosure relates to MHC class II-pos. antigen presenting cells contg. a specific regulator of Ii expression. Such cells are useful, for example, in the display of autodeterminant peptides in assocn. with MHC class II proteins. Compns. of the invention find application in methods for treating diseases, for example malignancies and autoimmune disorders, in a patient by enhancing immunol. attack on undesired cells. An addnl. application is the isolation of autodeterminant peptides from a cell.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:621103 CAPLUS
DOCUMENT NUMBER: 129:265463
TITLE: Down-regulation of gene expression by colorectal administration of synthetic oligonucleotides
INVENTOR(S): Zhang, Ruiwen; Agrawal, Sudhir
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840058	A2	19980917	WO 1998-US4914	19980312
WO 9840058	A3	19981119		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9865533	A1	19980929	AU 1998-65533	19980312
EP 1007098	A2	20000614	EP 1998-911615	19980312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527536	T2	20011225	JP 1998-539823	19980312

PRIORITY APPLN. INFO.:

US 1997-40738P	P	19970312
US 1997-846417	A	19970430

WO 1998-US4914 W 19980312

AB Disclosed is a method of down-regulating the expression of a gene in an animal, wherein an oligonucleotide complementary to the gene is colorectally administered to an animal. Also disclosed is a method for introducing an intact oligonucleotide into a mammal by colorectal administration, whereby the oligonucleotide is present in intact form in the systemic plasma of the mammal at least four hours following administration.

L11 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:467783 CAPLUS
DOCUMENT NUMBER: 127:104334
TITLE: Modified antisense oligonucleotides for inhibition of vascular endothelial growth factor synthesis for treatment of skin disorders
INVENTOR(S): Smyth, Adrienne P.; Robinson, Gregory S.
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720925	A1	19970612	WO 1996-US20441	19961206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5641756	A	19970624	US 1995-569926	19951208
AU 9716869	A1	19970627	AU 1997-16869	19961206

PRIORITY APPLN. INFO.:
US 1995-569926 A 19951208
US 1996-629730 A 19960409
US 1993-98942 A2 19930727
US 1995-378860 A2 19950126
US 1995-398945 A2 19950302
WO 1996-US20441 W 19961206

AB Modified oligonucleotides complementary to nucleotides in the region 58-90 of vascular endothelial growth factor (VEGF) gene that inhibit hypoxia or transforming growth factor .alpha. induction of VEGF synthesis are described for use in the treatment of proliferative disorders including those assocd. with neovascularization and angiogenesis, and psoriasis. The backbone of the oligonucleotide may include ribose, deoxyribose, or 2'-modified ribose, or phosphorothioate linkages. Antisense oligonucleotides of the invention inhibited VEGF synthesis and lowered levels of VEGF mRNA in tissue culture. Matrigel.RTM. implants of U373 glioblastoma cells showed lowered levels of vascularization and hemorrhage when anti-VEGF antisense oligonucleotides were incorporated into the matrix.

L11 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:569663 CAPLUS
DOCUMENT NUMBER: 125:214237
TITLE: Inhibition of neovascularization using vascular epidermal growth factor-specific oligonucleotides
INVENTOR(S): Robinson, Gregory S.; Smith, Lois Elaine Hodgson
PATENT ASSIGNEE(S): Hybridon, Inc., USA; Children's Medical Center Corporation

SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623065	A2	19960801	WO 1996-US1189	19960126
WO 9623065	A3	19960926		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD				
US 5731294	A	19980324	US 1995-378860	19950126
AU 9649074	A1	19960814	AU 1996-49074	19960126
AU 712579	B2	19991111		
EP 805858	A2	19971112	EP 1996-905270	19960126
EP 805858	B1	20010613		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11500426	T2	19990112	JP 1996-523058	19960126

PRIORITY APPLN. INFO.:
US 1995-378860 A 19950126
US 1993-98942 A2 19930727
WO 1996-US1189 W 19960126

AB Disclosed are methods of reducing neovascularization and of treating various disorders assocd. with neovascularization. These methods include administering to a tissue or subject a synthetic oligonucleotide specific for vascular endothelial growth factor nucleic acid effective in inhibiting the expression of vascular endothelial growth factor. Oligonucleotides effective in treating retinal neovascularization were synthesized and tested in vitro (in human cells) and in vivo (treatment of retinopathy of prematurity).

L11 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:380069 CAPLUS
DOCUMENT NUMBER: 125:27698
TITLE: Use of 2'-substituted antisense oligonucleotides to down-regulate gene expression
INVENTOR(S): Agrawal, Sudhir; Diasio, Robert B.; Zhang, Ruiwen
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612497	A1	19960502	WO 1995-US13069	19951017
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5591721	A	19970107	US 1994-328520	19941025
CA 2203652	AA	19960502	CA 1995-2203652	19951017
AU 9538930	A1	19960515	AU 1995-38930	19951017

EP 788366	A1	19970813	EP 1995-938213	19951017
EP 788366	B1	19991215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1170367	A	19980114	CN 1995-196839	19951017
JP 10507635	T2	19980728	JP 1995-513977	19951017
AT 187645	E	20000115	AT 1995-938213	19951017
ES 2141393	T3	20000316	ES 1995-938213	19951017
NO 9701905	A	19970624	NO 1997-1905	19970424
PRIORITY APPLN. INFO.:			US 1994-328520	19941025
			WO 1995-US13069	19951017

AB A method of down-regulating the expression of a gene in an animal using antisense oligonucleotides with non-phosphodiester bonds and a 2'-modified sugar forming the backbone is described. These oligonucleotide may be used in therapeutics and in research (as an alternative to prepg. knockout animals). A phosphorothioate oligonucleotide with 2'-O-methylribose was prepd. and administered to rats by gavage. Approx. 80% of the oligonucleotide was recovered in feces and urine and no degrdn. products were obtained from the stomach. Intact oligonucleotide was detected in the large intestine and blood plasma.

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L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:566652 CAPLUS
DOCUMENT NUMBER: 135:163318
TITLE: Human papillomavirus gene E1 antisense oligonucleotides for HPV inhibition, detection, and therapy
INVENTOR(S): Robert, Peter C.; Frank, Bruce L.; Szymkowski, David E.; Mills, John S.; Goodchild, John; Wolfe, Jia L.; Kilkuskie, Robert E.; Greenfield, Isobel M.; Sullivan, Veronia
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 471,974.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001010899	A1	20010802	US 1997-887497	19970702
US 2002068820	A1	20020606	US 1995-471974	19950606

PRIORITY APPLN. INFO.: US 1995-471974 A2 19950606
US 1996-21041P P 19960702

AB The present invention discloses synthetic oligonucleotides complementary to a nucleic acid spanning the translational start site of human papillomavirus gene E1,and including at least 15 nucleotides. Also disclosed are methods and kits for inhibiting the replication of HPV, for inhibiting the expression of HPV nucleic acid and protein, for detection of HPV, and for treating HPV infections. In some embodiments, these oligonucleotides are modified. In one embodiment, the modifications comprise at least one internucleotide linkage selected from the group consisting of **alkylphosphonate**, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester, including combinations of such linkages, as in a chimeric oligonucleotide. In other modifications, the oligonucleotides of the invention may also include at least one deoxyribonucleotide, at least one ribonucleotide, or a combination thereof, as in a hybrid oligonucleotide. In a particular embodiment, the oligonucleotide may consist of deoxyribonucleotides only. An oligonucleotide contg. at least one **2'-O-Me** ribonucleotide is one embodiment of the invention. Emphasis is given to oligonucleotides contg. phosphorothioate linkages, RNA-DNA hybrid regions, **2'-O-Me** RNA regions, 5-methyl-cytosine, amino propanol caps, **2'-O-Me** caps, and cholesteryl or polyethylene glycol linkers.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:116477 CAPLUS
DOCUMENT NUMBER: 126:114176
TITLE: Human papillomavirus inhibition and infection diagnosis and treatment using oligonucleotides complementary to gene E1 translation start site
INVENTOR(S): Frank, Bruce L.; Goodchild, John; Greenfield, Isobel M.; Kilkuskie, Robert E.; Mills, John S.; Roberts, Peter C.; Sullivan, Veronica; Szymkowski, David E.; Wolfe, Jia L.
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.; Hybridon Inc.
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639501	A2	19961212	WO 1996-EP2429	19960604
WO 9639501	A3	19970206		
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2002068820	A1	20020606	US 1995-471974	19950606
ZA 9604447	A	19961206	ZA 1996-4447	19960530
CA 2226457	AA	19961212	CA 1996-2226457	19960604
AU 9663002	A1	19961224	AU 1996-63002	19960604
EP 832214	A2	19980401	EP 1996-921927	19960604
EP 832214	B1	20001227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 198352	E	20010115	AT 1996-921927	19960604

PRIORITY APPLN. INFO.: US 1995-471974 A 19950606
WO 1996-EP2429 W 19960604

AB The present invention discloses synthetic oligonucleotides complementary to a nucleic acid spanning the translational start site of human papillomavirus gene E1, and including at least 15 nucleotides. Also disclosed are methods and kits for inhibiting the replication of HPV, for inhibiting the expression of HPV nucleic acid and protein, for detection of HPV, and for treating HPV infections. Emphasis is given to oligonucleotides contg. phosphorothioate linkages, RNA-DNA hybrid regions, **2'-O-Me** RNA regions, 5-methyl-cytosine, amino propanol caps, **2'-O-Me** caps, and cholesteryl or polyethylene glycol linkers.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:374664 CAPLUS
DOCUMENT NUMBER: 122:123152
TITLE: Oligonucleotide analogs containing ribonucleotide **alkylphosphonates** or alkylphosphonothioates and their use as pharmaceuticals
INVENTOR(S): Kandimalla, Ekambar R.; Temsamani, Jamal; Agrawal, Sudhir
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417093	A1	19940804	WO 1994-US902	19940125
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2154578	AA	19940804	CA 1994-2154578	19940125
AU 9461654	A1	19940815	AU 1994-61654	19940125
EP 677056	A1	19951018	EP 1994-908639	19940125
EP 677056	B1	19960522		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1121721	A	19960501	CN 1994-191393	19940125

AT 138384	E	19960615	AT 1994-908639	19940125
ES 2086997	T3	19960701	ES 1994-908639	19940125
JP 08508714	T2	19960917	JP 1994-517287	19940125
FI 9503541	A	19950831	FI 1995-3541	19950724
PRIORITY APPLN. INFO.:			US 1993-9262	19930125
			WO 1994-US902	19940125

AB Disclosed is an oligonucleotide analog comprising at least one ribonucleotide **alkylphosphonate** or alkylphosphonothioate. This analog is preferably from 2 to 60 nucleotides in length and has at least one ribonucleotide substituted at the 2' position of its ribose group. Also disclosed are therapeutic formulations comprising this oligonucleotide analog, methods of inhibiting the expression of a gene from a virus, pathogenic organism, or cell, the expression of which is assocd. with a disease state, and methods of treating a mammal infected with a virus or pathogenic organism or afflicted with a disorder resulting from the expression of a cellular gene. Oligonucleotide CTCTCGCACCCATCTCTCTCCUUCT, contg. methylphosphonate linkages between the first 20 nucleotides and phosphodiester linkages between the remaining nucleotides and contg. **2'-O-Me** groups on residues 21-24, was prepd. and characterized. The methylphosphonate modification did not hinder duplex formation with complementary DNA or RNA nor did it significantly destabilize the duplexes formed. The modified oligonucleotide was 8-9-fold more resistant to snake venom phosphodiesterase than was the control oligonucleotide.

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L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:53549 CAPLUS
DOCUMENT NUMBER: 118:53549
TITLE: **2'-O-alkyl**
-oligoribonucleotides, their synthesis and use in antisense oligonucleotides
INVENTOR(S): Brunar, Helmut; Holzner, Armin; Issakides, Georg; Knollmueller, Max; Noe, Christian; Birnstiel, Max; Cotten, Matthew; Oberhauser, Bernd; Wagner, Ernst; Schaffner, Gotthold
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4110085	A1	19921001	DE 1991-4110085	19910327

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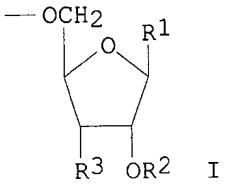

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AB Oligoribonucleotides contg. 3-35 **2'-O-alkyl** **ribonucleotides** (I, R1 = uracilyl, adenyl, guanyl, inosinyl; R2 = C1-C30 alkyl; R3 = phosphate diester, **methylphosphonate**, phosphoramidate, phosphorothioate), and free 3' and 5' hydroxyls or phosphate esters, or terminated with a marking group or lipophilic group, are claimed. These oligoribonucleotides are more effective as antisense RNAs than are those not contg. the modified bases. Expts. in which such oligonucleotides are shown to be more effective inhibitors of histone H4 mRNA processing with inhibition less easily reversed are reported. A 19-mer contg. O-alkyl **ribonucleotides** was at least as effective an inhibitor of the processing reaction as a 63-mer not contg. the modified nucleotides.

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:205352 CAPLUS
DOCUMENT NUMBER: 130:237810
TITLE: Preparation of mixed backbone **antisense** oligodeoxyribonucleotides containing 2'-5'-ribonucleotides and 3'-5'-deoxyribonucleotides as antitumors and virucides
INVENTOR(S): Kandimalla, Ekambar R.; Agrawal, Sudhir
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5886165	A	19990323	US 1996-719970	19960924

AB The present invention provides a novel class of oligonucleotides useful for **antisense** purposes. The oligonucleotides of the invention comprise both deoxyribonucleotides with "natural" 3'-5' **internucleotide linkages** and ribonucleotides with 2'-5' **internucleotide linkages**. Because of their conformation structure, oligonucleotides according to the invention possess uniform intra-phosphate distances throughout the oligonucleotide chain, allowing them to bind efficiently to complementary DNA and RNA with "natural" 3'-5' **internucleotide linkages**. The oligodeoxyribonucleotides according to the invention advantageously exhibit diminished immune stimulation and significantly reduced effect on both complement and coagulation as compared to 3'-5'-oligodeoxyribonucleotides.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:567887 CAPLUS
DOCUMENT NUMBER: 129:299001
TITLE: Study of phosphorothioate-modified oligonucleotide resistance to 3'-exonuclease using capillary electrophoresis
AUTHOR(S): Gilar, Martin; Belenky, Alexei; Budman, Yeva; Smisek, David L.; Cohen, Aharon S.
CORPORATE SOURCE: Hybridon, Inc., 620 Memorial Drive, Cambridge, MA, 02139, USA
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1998), 714(1), 13-20
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of phosphorothioate (PS) **internucleotide linkages** on the stability of phosphodiester oligodeoxyribonucleotides (ODNs) was investigated using 25-mer ODNs contg. single or multiple PS backbone modifications. The in vitro stability of the oligomers was measured both in 3'-exonuclease soln. and in plasma. For the sepn. of ODNs, capillary electrophoresis with a replaceable polymer sepn. matrix was used. As expected, DNA fragments with PS linkages at the 3'-end were found to be more resistant to 3'-exonuclease hydrolysis. Also increasing exonuclease resistance was the non-specific adsorption of phosphorothioate ODNs to enzyme.

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:313808 CAPLUS
DOCUMENT NUMBER: 127:28622

TITLE: Effects of synthetic oligonucleotides on human complement and coagulation

AUTHOR(S): Shaw, Denise R.; Rustagi, Pradip K.; Kandimalla, Ekambar R.; Manning, Adrienne N.; Jiang, Zhiwei; Agrawal, Sudhir

CORPORATE SOURCE: DEPARTMENT OF MEDICINE, DIVISION OF HEMATOLOGY AND ONCOLOGY, UNIVERSITY OF ALABAMA AT BIRMINGHAM, BIRMINGHAM, AL, 35294, USA

SOURCE: Biochemical Pharmacology (1997), 53(8), 1123-1132
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Oligodeoxynucleotide phosphorothioates (PS-oligos) are being studied as novel therapeutic agents based on their ability to inhibit gene expression. Preclin. studies produced unanticipated complement and coagulation effects in monkeys receiving high-dose PS-oligo. In the present in vitro studies, PS-oligo inhibited normal human blood clotting as well as subsequent assays for prothrombin fragment PF1+2 and hemolytic complement. PS-oligo treatment of normal donor plasma produced concn.-dependent prolongations of clotting times, with the activated partial thromboplastin time more sensitive than prothrombin time or thrombin clotting time. PS-oligo treatment of normal donor serum similarly reduced hemolytic complement activity in a concn.-dependent manner. Reduced hemolysis correlated with increased levels of complement fragment C4d. The anti-heparin drug protamine sulfate inhibited in vitro effects of PS-oligo in both complement and coagulation assays, suggesting that charged residues in **internucleotide linkages** of PS-oligo mediated the obsd. activities. Therefore, oligonucleotides with varying **internucleotide linkages**, nucleotide sequence, or secondary structure were compared. Both complement and coagulation effects appeared to be independent of nucleotide sequence but were strongly related to the nature of **internucleotide linkages**. Several of these modified oligonucleotides have been shown previously to retain potent **antisense** activity and thus may represent viable alternatives for **antisense** therapeutics.

L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:756391 CAPLUS

DOCUMENT NUMBER: 123:135101

TITLE: Method for detecting charged oligonucleotides in biological fluids

INVENTOR(S): Cohen, Aharon S.; Bourque, Andre

PATENT ASSIGNEE(S): Hybridon, Inc., USA

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514087	A1	19950526	WO 1994-US13061	19941115
W: AM, AT, AU, BB, BG, BR, BY, CA, CN, CZ, DE, DK, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5506103	A	19960409	US 1993-153365	19931116
CA 2176341	AA	19950526	CA 1994-2176341	19941115
AU 9510554	A1	19950606	AU 1995-10554	19941115
EP 729510	A1	19960904	EP 1995-901235	19941115

EP 729510	B1	19970806			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09505402	T2	19970527	JP 1994-514530	19941115	
AT 156516	E	19970815	AT 1995-901235	19941115	
PRIORITY APPLN. INFO.:			US 1993-153365	19931116	
			WO 1994-US13061	19941115	

AB Disclosed is a method for detecting and quantitating oligonucleotides with charged **internucleotide linkages** in biol. fluids. In this method, a biol. fluid sample is contacted with an anion exchange resin at from 40 .degree.C to 65 .degree.C for a time sufficient to enable oligonucleotides in the sample to adsorb to the resin. The adsorbed oligonucleotides are then desorbed with a buffer having a salt concn. of about 1 M to 2.5 M and a pH in the range of about 6.5 to 7.5, the desorption being performed at about 40 - 65 .degree.C. The oligonucleotides so released are then detected and quantitated.

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:501227 CAPLUS
DOCUMENT NUMBER: 121:101227
TITLE: Therapeutic anti-HIV oligonucleotide and pharmaceutical
INVENTOR(S): Agrawal, Sudhir; Tang, Jin Yan
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9408004	A1	19940414	WO 1993-US9392	19931004
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, LV, NO, NZ, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, PT, SE				
EP 664833	A1	19950802	EP 1993-924289	19931004
EP 664833	B1	19961227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 72400	A2	19960429	HU 1995-995	19931004
JP 08504570	T2	19960521	JP 1993-509354	19931004
AT 146819	E	19970115	AT 1993-924289	19931004
ES 2096343	T3	19970301	ES 1993-924289	19931004
AU 678415	B2	19970529	AU 1994-54028	19931004
BR 9307191	A	19990330	BR 1993-7191	19931004
US 5684147	A	19971104	US 1994-319823	19941007
FI 9501600	A	19950510	FI 1995-1600	19950404
NO 9501307	A	19950601	NO 1995-1307	19950404
PRIORITY APPLN. INFO.:			US 1992-958135	19921005
			WO 1993-US9392	19931004

AB Disclosed are oligonucleotides having nucleotide sequences that hybridize to at least nucleotides 324 to 348 of a conserved gag region of the HIV-1 genome. These oligonucleotides have about 25 to 30 nucleotides linked by at least one non-phosphodiester **internucleotide linkage** which render them resistant to nuclease digestion. Also disclosed are therapeutic formulations contg. such oligonucleotides and methods of inhibition HIV-1 proliferation and of treating HIV-1 infection in a mammal. Phosphorothioate-modified oligodeoxynucleotides 25-30 nucleotide in length which hybridize to the specified region of the HIV-1 genome were shown to be more effective that a 20-mer complementary to 327-346 or a 28-mer complementary to only a fragment of the 324-348 region. Syncytia formation, p24 expression, cytopathic effect, and reverse transcriptase activity were monitored to assay the effects of the **antisense** oligonucleotides.

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:811814 CAPLUS
DOCUMENT NUMBER: 128:154339
TITLE: Sequencing of modified oligonucleotides using in-source fragmentation and delayed pulsed ion extraction matrix-assisted laser desorption ionization time-of-flight mass spectrometry
AUTHOR(S): Wang, Bing H.; Hopkins, Christopher E.; Belenky, Alexei B.; Cohen, Aharon S.
CORPORATE SOURCE: Analytical Research, Hybridon, Inc., Cambridge, MA, 02139, USA
SOURCE: International Journal of Mass Spectrometry and Ion Processes (1997), 169/170, 331-350
CODEN: IJMPDN; ISSN: 0168-1176
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOFMS) was used to sequence modified oligonucleotides (MONs). Under delayed pulsed ion extn. conditions, sequence ions of MONs resulting from fragmentation within the ion source can be obsd. In this work, several common types of **antisense** MONs with sizes up to 25-mer were studied including an oligodeoxynucleotide (ODN) of phosphorothioate-phosphodiester (PS-PO) chimera, an all PS ODN, a partially 2'-O-methylated all PS oligodeoxyribonucleotide-oligoribonucleotide (ODN-ON) chimera, and an ODN of phosphorothioate-**methylphosphonate** (PS-MP) chimera. The sequence ions obsd. include 'w', 'd', as well as hitherto little discussed 'a' and 'z' ions. While a complete sequence can be constructed from 'w' ions for chimeric PS-PO ODN, all PS ODN, and chimeric PS ODN-ON, 'a' ions or 'd' ions provide useful supplemental information. For the PS-MP ODN, however, 'd' ions are crit. in filling the gap in the sequence constructed from 'w' ions. The method provides a rapid quality control tool in oligonucleotide synthesis allowing sequence verification to be accomplished in minutes rather than hours needed by chem. or enzymic methods. The observation that the fragmentation pattern in the PS ON region is rather similar to that of PS ODN together with the observation of 'a' ions suggests that backbone cleavage pathways may not always involve nucleobases losses. Fragmentation mechanisms alternative to those found in MALDI-TOFMS literature have been proposed.

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:757784 CAPLUS
DOCUMENT NUMBER: 128:97324
TITLE: Mixed - backbone oligonucleotides containing phosphorothioate and **methylphosphonate** linkages as second generation **antisense** oligonucleotide
AUTHOR(S): Agrawal, Sudhir; Jiang, Zhiwei; Zhao, Qiuyan; Shaw, Denise; Sun, Daisy; Saxinger, Carl
CORPORATE SOURCE: Hybridon, Inc, Worcester, MA, 01605, USA
SOURCE: Nucleosides & Nucleotides (1997), 16(7-9), 927-936
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Antisense** oligonucleotides are being studied as novel therapeutic agents. To further improve the properties of **antisense** oligonucleotides, we have synthesized phosphorothioate oligonucleotides contg. **methylphosphonate** linkages at the 5'-end, the 3'-end, or in the center, and have evaluated the impact of these linkages on the biophys. properties, biol. properties, and some of the safety parameters.

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:496124 CAPLUS
DOCUMENT NUMBER: 125:184810
TITLE: Pharmacokinetics and tissue disposition of a chimeric oligodeoxynucleoside phosphorothioate in rats after intravenous administration
AUTHOR(S): Zhang, Ruiwen; Iyer, Radhakrishnan P.; Yu, Dong; Tan, Weitian; Zhang, Xueshu; Lu, Zhihong; Zhao, Hui; Agrawal, Sudhir
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Alabama, Birmingham, AL, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 278(2), 971-979
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Antisense** oligonucleotides represent a novel therapeutic principle for designing drugs against various diseases. Oligonucleotides can be chem. modified to improve their pharmacokinetics and in vivo stability, and it is important to understand the effect of these modifications. In the present study,the pharmacokinetics of a 25-mer phosphorothioate oligonucleotide contg. four contiguous, internucleotide, **methylphosphonate** linkages at the 3'- and 5'-ends (chimeric oligonucleotide) were detd. in rats after i.v. administration of the 35S-labeled oligonucleotide at a dose of 30 mg/kg. Plasma disappearance of the oligonucleotide could be described by a two-compartment model, with half-lives of 0.38 and 52.9 h. The intact chimeric oligonucleotide was detected in plasma up to 6 h after dosing. Urinary excretion represented the major elimination pathway, with approx. 21% of the administered dose being excreted within 24 h and 35% being excreted over a 240-h period after dosing. The majority of the radioactivity in urine was assocd. with the intact oligonucleotide within 6 h after dosing and with increasing degrdn. products thereafter. Fecal excretion was a minor elimination pathway. The oligonucleotide was widely distributed in tissues, with the majority of the radioactivity in most tissues being intact up to 48 h after dosing. Compared with oligodeoxynucleotide phosphorothioates, the chimeric oligonucleotide was significantly more stable in vivo. The presence of intact oligonucleotide in plasma and tissues even 12 h after dosing is a significant advantage over an "all"-phosphorothioate analog. Thus, the chimeric oligonucleotide could provide a longer duration of action as an **antisense** agent after its administration.

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:121840 CAPLUS
DOCUMENT NUMBER: 124:277954
TITLE: Novel enzymic and immunological responses to oligonucleotides
AUTHOR(S): Agrawal, Sudhir; Rustagi, Pradip K.; Shaw, Denise R.
CORPORATE SOURCE: Hybridon, Inc., One Innovation Drive, Worcester, MA, 01605, USA
SOURCE: Toxicology Letters (1995), 82/83(1-6), 431-4
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oligonucleotide phosphorothioates (PS-oligos) are being studied as **antisense** agents for viral infection and cancer. In preclin. studies, PS-oligos produced dose-dependent changes in heart rate and blood pressure and significantly reduced serum hemolytic complement, which could be avoided by slowing infusion rates. Here, in vitro PS-oligo treatment of either human, rhesus monkey or guinea pig serum reduced hemolytic complement and further inhibited in vitro coagulation when added to whole blood or citrated plasma. These effects were dependent upon both

oligonucleotide dose and structure. Oligonucleotides having identical sequences but contg. **methylphosphonates** (Chimeric), 2'-O-Me ribonucleosides (Hybrid) or 3' hairpin loop (Self-stabilized) had altered effects on complement and coagulation in vitro.

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1995:631138 CAPLUS
DOCUMENT NUMBER:	123:314354
TITLE:	Synthesis and properties of 2'-O-methylribonucleotide **methylphosphonate** containing chimeric oligonucleotides
AUTHOR(S):	Kandimalla, Ekambar R.; Temsamani, Jamal; Agrawal, Sudhir
CORPORATE SOURCE:	Hybridon, Inc., Worcester, MA, 01605, USA
SOURCE:	Nucleosides & Nucleotides (1995), 14(3-5), 1031-5 CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER:	Dekker
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB 2'-O-methylribonucleoside methylphosphonamidites and synthesized and incorporated into oligonucleotides to obtain chimeric **antisense** oligonucleotides. The resulting oligonucleotide binds to their target RNA/DNA sequences efficiently and stable in a medium contg. bovine serum.